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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/12, C07K 14/47, C12N 15/11, C12Q 1/68, C07K 16/18, G01N 33/68, A61K 38/17		A3	(11) International Publication Number: WO 00/00610 (43) International Publication Date: 6 January 2000 (06.01.00)																												
(21) International Application Number: PCT/US99/14484 (22) International Filing Date: 25 June 1999 (25.06.99) (30) Priority Data: <table><tr><td>60/090,762</td><td>26 June 1998 (26.06.98)</td><td>US</td></tr><tr><td>60/094,983</td><td>31 July 1998 (31.07.98)</td><td>US</td></tr><tr><td>60/102,686</td><td>1 October 1998 (01.10.98)</td><td>US</td></tr><tr><td>60/112,129</td><td>11 December 1998 (11.12.98)</td><td>US</td></tr></table> (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications <table><tr><td>US</td><td>60/090,762 (CIP)</td></tr><tr><td>Filed on</td><td>26 June 1998 (26.06.98)</td></tr><tr><td>US</td><td>60/094,983 (CIP)</td></tr><tr><td>Filed on</td><td>31 July 1998 (31.07.98)</td></tr><tr><td>US</td><td>60/102,686 (CIP)</td></tr><tr><td>Filed on</td><td>1 October 1998 (01.10.98)</td></tr><tr><td>US</td><td>60/112,129 (CIP)</td></tr><tr><td>Filed on</td><td>11 December 1998 (11.12.98)</td></tr></table> (71) Applicant (for all designated States except US): INCYTE PHARMACEUTICALS, INC. [US/US]; 3174 Porter Drive, Palo Alto, CA 94304 (US).		60/090,762	26 June 1998 (26.06.98)	US	60/094,983	31 July 1998 (31.07.98)	US	60/102,686	1 October 1998 (01.10.98)	US	60/112,129	11 December 1998 (11.12.98)	US	US	60/090,762 (CIP)	Filed on	26 June 1998 (26.06.98)	US	60/094,983 (CIP)	Filed on	31 July 1998 (31.07.98)	US	60/102,686 (CIP)	Filed on	1 October 1998 (01.10.98)	US	60/112,129 (CIP)	Filed on	11 December 1998 (11.12.98)	(72) Inventors; and (75) Inventors/Applicants (for US only): LAL, Preeti [IN/US]; 2382 Lass Drive, Santa Clara, CA 95054 (US). TANG, Y., Tom [CN/US]; 4230 Ranwick Court, San Jose, CA 95118 (US). GORGONE, Gina, A. [US/US]; 1253 Pinecrest Drive, Boulder Creek, CA 95006 (US). CORLEY, Neil, C. [US/US]; 1240 Dale Avenue #30, Mountain View, CA 94040 (US). GUEGLER, Karl, J. [CH/US]; 1048 Oakland Avenue, Menlo Park, CA 94025 (US). BAUGHN, Mariah, R. [US/US]; 14244 Santiago Road, San Leandro, CA 94577 (US). AKERBLOM, Ingrid, E. [US/US]; 1234 Johnson Street, Redwood City, CA 94061 (US). AU-YOUNG, Janice [US/US]; 1419 Kains Avenue, Berkeley, CA 94702 (US). YUE, Henry [US/US]; 826 Lois Avenue, Sunnyvale, CA 94087 (US). PATTERSON, Chandra [US/US]; 490 Sherwood Way #1, Menlo Park, CA 94025 (US). REDDY, Roopa [IN/US]; 1233 W. McKinley Drive, Sunnyvale, CA 94086 (US). HILLMAN, Jennifer, L. [US/US]; 230 Monroe Drive #12, Mountain View, CA 94040 (US). BANDMAN, Olga [US/US]; 366 Anna Avenue, Mountain View, CA 94043 (US). (74) Agents: BILLINGS, Lucy, J. et al.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 29 June 2000 (29.06.00)	
60/090,762	26 June 1998 (26.06.98)	US																													
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(54) Title: HUMAN SIGNAL PEPTIDE-CONTAINING PROTEINS																															
(57) Abstract <p>The invention provides human signal peptide-containing proteins (HSPP) and polynucleotides which identify and encode HSPP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of HSPP.</p>																															

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EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/ 14484

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim 19 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 17, 18, 20
because they relate to parts of the international Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see additional sheet, subject 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Further defect(s) under Article 17(2)(a):

Continuation of Box 3.

Claims Nos.: 17,18,20

Claims 17,18 and 20 refer to antagonists and agonists of the polypeptides without giving a true technical characterization. Moreover, no such specific compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6, PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of, claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

INVENTION 1: Claims 1-20 (all partially)

A polypeptide comprising the amino acid sequence of SEQ.ID.1 and variants having at least 90% amino acid sequence identity therewith; the polynucleotide encoding said polypeptide (as represented by SEQ.ID.135) and variants having at least 90% sequence identity with said polynucleotide; a polynucleotide that hybridizes therewith or a polynucleotide that is complementary thereto; a method for detecting said polynucleotide, an expression vector comprising said polynucleotide; a host cell comprising said vector; a method for producing said polypeptide; a pharmaceutical composition comprising said polypeptide; a purified antibody, agonist or antagonist specific for said polypeptide; and a method for treating or preventing a disorder associated with decreased or increased expression of said polypeptide.

INVENTIONS 2-134: Claims 1-20 (all partially)

Idem as subject 1 but limited to one DNA sequence selected from SEQ.IDs. 136-268 at a time and the corresponding polypeptide, where invention 2 is limited to SEQ.IDs. 136 and 2, invention 3 is limited to SEQ.IDs. 137 and 3, and invention 134 is limited to SEQ.IDs. 268 and 134.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/14484

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0607054 A	20-07-1994	CA 2113363 A	15-07-1994
		JP 2879303 B	05-04-1999
		JP 6315380 A	15-11-1994
		JP 11308993 A	09-11-1999
		US 5525486 A	11-06-1996

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PF-0541 PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below	
International application No. PCT/US 99/ 14484	International filing date (day/month/year) 25/06/1999	(Earliest) Priority Date (day/month/year) 26/06/1998
Applicant INCYTE PHARMACEUTICALS, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38 2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention

☐ None of the figures

INTERNATIONAL SEARCH REPORT

International application No

PCT/US 99/ 14484

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

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1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claim 19 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 17, 18, 20
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see additional sheet, subject 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Further defect(s) under Article 17(2)(a):

Continuation of Box 3.

Claims Nos.: 17,18,20

Claims 17,18 and 20 refer to antagonists and agonists of the polypeptides without giving a true technical characterization. Moreover, no such specific compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6, PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of, claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

INVENTION 1: Claims 1-20 (all partially)

A polypeptide comprising the amino acid sequence of SEQ.ID.1 and variants having at least 90% amino acid sequence identity therewith; the polynucleotide encoding said polypeptide (as represented by SEQ.ID.135) and variants having at least 90% sequence identity with said polynucleotide; a polynucleotide that hybridizes therewith or a polynucleotide that is complementary thereto; a method for detecting said polynucleotide, an expression vector comprising said polynucleotide; a host cell comprising said vector; a method for producing said polypeptide; a pharmaceutical composition comprising said polypeptide; a purified antibody, agonist or antagonist specific for said polypeptide; and a method for treating or preventing a disorder associated with decreased or increased expression of said polypeptide.

INVENTIONS 2-134: Claims 1-20 (all partially)

Idem as subject 1 but limited to one DNA sequence selected from SEQ.IDs. 136-268 at a time and the corresponding polypeptide, where invention 2 is limited to SEQ.IDs. 136 and 2, invention 3 is limited to SEQ.IDs. 137 and 3, and invention 134 is limited to SEQ.IDs. 268 and 134.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 99/14484

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C07K14/47 C12N15/11 C12Q1/68 C07K16/18
G01N33/68 A61K38/17

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K C12Q G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HUDSON T.: "Human STS." EMBL DATABASE ENTRY HS578357, ACCESSION NUMBER G22578, 1 June 1996 (1996-06-01), XP002125359 abstract	5
A	--- TASHIRO K. ET AL.: "SIGNAL SEQUENCE TRAP: A CLONING STRATEGY FOR SECRETED PROTEINS AND TYPE I MEMBRANE PROTEINS" SCIENCE, vol. 261, 1993, pages 600-603, XP002911163 ISSN: 0036-8075 the whole document	1-16,19
A	--- EP 0 607 054 A (HONJO TASUKU ;ONO PHARMACEUTICAL CO (JP)) 20 July 1994 (1994-07-20) the whole document --- -/--	1-16,19

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

20 December 1999

Date of mailing of the international search report

05 04 2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Mandl, B

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/14484

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JACOBS K. A. ET AL: "A genetic selection for isolating cDNAs encoding secreted proteins" GENE, vol. 198, 1997, pages 289-296, XP002102962 ISSN: 0378-1119 the whole document ---	1-16,19
A	WALLIN E. ET AL.: "Properties of N-terminal tails in G-protein coupled receptors: a statistical study" PROTEIN ENGINEERING, vol. 8, no. 7, 1995, pages 693-698, XP002102961 ISSN: 0269-2139 the whole document -----	1-16,19

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/14484

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0607054 A	20-07-1994	CA 2113363 A	15-07-1994
		JP 2879303 B	05-04-1999
		JP 6315380 A	15-11-1994
		JP 11308993 A	09-11-1999
		US 5525486 A	11-06-1996

TENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 10 October 2000 (10.10.00)	
International application No. PCT/US99/14484	Applicant's or agent's file reference PF-0541 PCT
International filing date (day/month/year) 25 June 1999 (25.06.99)	Priority date (day/month/year) 26 June 1998 (26.06.98)
Applicant LAL, Preeti et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 20 January 2000 (20.01.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Kiwa Mpay Telephone No.: (41-22) 338.83.38
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